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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,738	12/08/2000	William Peter Van Antwerp	G&C 130.9-US-U1	4789

22462 7590 11/29/2002

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EXAMINER

LUKTON, DAVID

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 11/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/733,738

Applicant(s)

VAN ANTWERP ET AL.

Examiner

David Lukton

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 1-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5, 7.

- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Applicants' election of Group 4 with traverse is acknowledged.

Also acknowledged are applicants' species elections (Lys^{B28}, Pro^{B29} human insulin is the peptide of interest, phosphate is present, zinc is present, glycerol is present, and corresponds to the "isotonicity agent")

Applicants have traversed the restriction by arguing essentially that once a complete search of the Group 4 invention has been completed, the additional burden to search the invention of Groups 1-3 would be minimal. However, this is not the case at all. First, claim 1 does not require the presence of a "phenolic preservative". To search for all possible embodiments would do not require the presence of a "phenolic preservative" would require a far greater undertaking than if a "phenolic preservative" must be present. Claim 1 also does not require zinc. Second, claim 1 would encompass solutions which have been prepared for reasons other than minimization of aggregation. Some investigators prepare solutions for immediate use. Accordingly, the limitations in claim 19 are vastly greater than they are in claim 1. It is certainly not the case that a thorough search of the claim 19 invention would mean that little additional searching would be required for claim 1. The restriction requirement is still deemed to be proper.

※

Claims 19-24 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In claim 19, line 1, the term "the peptide" lacks antecedent basis.
- Claim 19 is indefinite as to the process steps and endpoint. What are the criteria for stabilization? Suppose that there were two solutions, solution #1, and solution #2. The first solution is prepared by combining insulin with the mixed buffer system in which the Tris is present at the nanomolar concentration range and as such contributes nothing to the buffering capacity of the solution; in solution #1 the stoichiometry of insulin to zinc is 1000:1. In solution #2, the amounts of the various reagents are such as to minimize aggregation. If a chemist were to use solution #1, how would he achieve stabilization, and what would be the evidence of such. The following format is suggested:

A method of inhibiting aggregation of a polypeptide comprising combining the polypeptide with a ... buffer... for a time and under conditions effective to inhibit aggregation.

- Claim 19 recites that the buffering molecule "counteracts" carbon dioxide. What is meant by this? Does this mean mitigating the change in pH that results from the formation of carbonic acid?
- In claim 19, the abbreviation "Tris" may be used if accompanied by the full name that this abbreviation represents.

※

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention

was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 19-21, 23-24 are rejected under 35 U.S.C. §103 as being unpatentable over Massey (USP 4,849,341).

Massey discloses solutions for stabilizing insulin. The solutions contain Tris (col 4, line 41) and glycerol (col 4, line 48+ and tables 1-2). Although phosphate is mentioned (col 4, line 40) as a possible component of the solution, the reference does not mandate its presence. However, phosphate is a common buffer, and one would have been motivated to use the phosphate to increase buffering capacity.

It is noted that Massey requires the presence of a polyethylene glycol polypropylene glycol polymer, which is not required by the instant claims. However, the "buffer system" of the instant claims "comprise" any compound in addition to those specified.

Thus, the claims are rendered obvious.

*

Claim 19 is rejected under 35 U.S.C. §103 as being unpatentable over Langballe (USP

6,174,856)

Langballe discloses a method of stabilizing insulin.

The solution may contain at least one buffer selected from Gly-Gly, Tris, and citrate. Thus, for the chemist endeavoring to use more than one such buffer, there are three such possibilities: Gly-Gly and Tris, Tris and citrate, Gly-Gly and citrate.

Also disclosed (col 5, line 64+) the use of an "additional buffer". Thus, there is motivation to use two different buffers. In addition, it is recited (col 5, line 66+) that citrate can serve the role of a buffer or a zinc complexing agent. Furthermore, it is disclosed (col 6, line 29) that when zinc was used, it was added as the "acetate". Thus, a practitioner might choose Tris in combination with citrate to complex the zinc, or the practitioner might simply select Tris as the only buffer, but then use zinc acetate, thus meeting the requirement for the second buffer.

Thus, the claim is rendered obvious.

✱

JP 57067548 A was stricken from the IDS because of the absence of a translation.

No claim is allowed.

Serial No. 09/733,738
Art Unit 1653

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



**DAVID LUKTON
PATENT EXAMINER
GROUP 1800**